

FORM PTO-1390 (Modified)  
(REV. 11-98)

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER

TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED/ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371

203 Von Bezold

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR

09/581103

INTERNATIONAL APPLICATION NO.

PCT/EP 98/07952

INTERNATIONAL FILING DATE

08/12/1998

PRIORITY DATE CLAIMED

08/12/97

TITLE OF INVENTION

DEVICE AND PROCEDURE FOR IMAGE RECORDING ON DROP-GENERATING DISPENSING HEADS

APPLICANT(S) FOR DO/EO/US

Markus Kietzmann and Holger Eickhoff

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
  - a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
  - b. ☐ has been transmitted by the International Bureau.
  - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ A copy of the International Search Report (PCT/ISA/210).
8. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
  - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
  - b. ☐ have been transmitted by the International Bureau.
  - c. ☒ have not been made; however, the time limit for making such amendments has NOT expired.
  - d. ☐ have not been made and will not be made.
9. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
10. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
11. ☒ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

## Items 13 to 20 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter.
19. ☒ Certificate of Mailing by Express Mail
20. ☐ Other items or information:

U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 1.53) <b>09/581103</b>		INTERNATIONAL APPLICATION NO. <b>PCT/EP 98/07952</b>		ATTORNEY'S DOCKET NUMBER <b>203 Von Bezold</b>	
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21. The following fees are submitted:

<b>BASIC NATIONAL FEE ( 37 CFR 1.492 (a) (1) - (5)) :</b>				<b>CALCULATIONS PTO USE ONLY</b>	
<input type="checkbox"/> Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO .....	<b>\$970.00</b>				
<input checked="" type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO .....	<b>\$840.00</b>				
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO .....	<b>\$690.00</b>				
<input type="checkbox"/> International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) .....	<b>\$670.00</b>				
<input type="checkbox"/> International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) .....	<b>\$96.00</b>				
<b>ENTER APPROPRIATE BASIC FEE AMOUNT =</b>		<b>\$840.00</b>			
Surcharge of <b>\$130.00</b> for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).		<b>\$0.00</b>			
<b>CLAIMS</b>	<b>NUMBER FILED</b>	<b>NUMBER EXTRA</b>	<b>RATE</b>		
Total claims	12 - 20 =	0	x \$18.00	<b>\$0.00</b>	
Independent claims	1 - 3 =	0	x \$78.00	<b>\$0.00</b>	
Multiple Dependent Claims (check if applicable). <input type="checkbox"/>				<b>\$0.00</b>	
<b>TOTAL OF ABOVE CALCULATIONS =</b>				<b>\$840.00</b>	
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28) (check if applicable). <input type="checkbox"/>				<b>\$0.00</b>	
<b>SUBTOTAL =</b>				<b>\$840.00</b>	
Processing fee of <b>\$130.00</b> for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).				<b>\$0.00</b>	
<b>TOTAL NATIONAL FEE =</b>				<b>\$840.00</b>	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable). <input type="checkbox"/>				<b>\$0.00</b>	
<b>TOTAL FEES ENCLOSED =</b>				<b>\$840.00</b>	
				<b>Amount to be: refunded</b>	\$
				<b>charged</b>	\$

☒ A check in the amount of **\$840.00** to cover the above fees is enclosed.

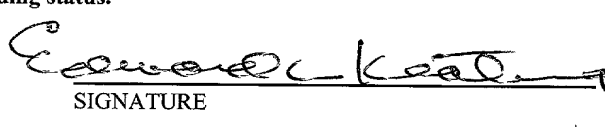
☐ Please charge my Deposit Account No. \_\_\_\_\_ in the amount of \_\_\_\_\_ to cover the above fees.  
A duplicate copy of this sheet is enclosed.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. **11-1013** A duplicate copy of this sheet is enclosed.

**NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.**

SEND ALL CORRESPONDENCE TO:

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 SIGNATURE  
**Edward M. Keating**  
 NAME  
**20,646**  
 REGISTRATION NUMBER  
**June 8, 2000**  
 DATE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

**STATEMENT CLAIMING SMALL ENTITY STATUS**  
**(37 CFR 1.9(f) & 1.27(d))—NONPROFIT ORGANIZATION**

Docket Number (Optional)  
203 VonBez

Applicant, Patentee, or Identifier: Markus KIETZMANN et al.

Application or Patent No.: \_\_\_\_\_

Filed or Issued: \_\_\_\_\_

Title: Device and Procedure for Image Recording on Drop-Generating Dispensing Heads

I hereby state that I am an official empowered to act on behalf of the nonprofit organization identified below:

NAME OF NONPROFIT ORGANIZATION Max-Planck-Gesellschaft zur Förderung der  
ADDRESS OF NONPROFIT ORGANIZATION Wissenschaften e.V.,  
Hofgartenstraße 8, D-80539 München (Germany)

**TYPE OF NONPROFIT ORGANIZATION:**

- ☐ UNIVERSITY OR OTHER INSTITUTION OF HIGHER EDUCATION
- ☐ TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE (26 U.S.C. 501(a) and 501(c)(3))
- ☐ NONPROFIT SCIENTIFIC OR EDUCATIONAL UNDER STATUTE OF STATE OF THE UNITED STATES OF AMERICA  
(NAME OF STATE \_\_\_\_\_)  
(CITATION OF STATUTE \_\_\_\_\_)
- ☒ WOULD QUALIFY AS TAX EXEMPT UNDER INTERNAL REVENUE SERVICE CODE (26 U.S.C. 501(a) and 501(c)(3))  
IF LOCATED IN THE UNITED STATES OF AMERICA
- ☐ WOULD QUALIFY AS NONPROFIT SCIENTIFIC OR EDUCATIONAL UNDER STATUTE OF STATE OF THE UNITED STATES OF AMERICA IF LOCATED IN THE UNITED STATES OF AMERICA  
(NAME OF STATE \_\_\_\_\_)  
(CITATION OF STATUTE \_\_\_\_\_)

I hereby state that the nonprofit organization identified above qualifies as a nonprofit organization as defined in 37 CFR 1.9(e) for purposes of paying reduced fees to the United States Patent and Trademark Office regarding the invention described in:

- ☐ the specification filed herewith with title as listed above.
- ☐ the application identified above.
- ☐ the patent identified above.

I hereby state that rights under contract or law have been conveyed to and remain with the nonprofit organization regarding the above identified invention. If the rights held by the nonprofit organization are not exclusive, each individual, concern, or organization having rights in the invention must file separate statements as to their status as small entities and that no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent inventor under 37 CFR 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern, or organization having any rights in the invention is listed below:

- ☐ no such person, concern, or organization exists.
- ☐ each such person, concern, or organization is listed below.

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

NAME OF PERSON SIGNING Christa Herzog

TITLE IN ORGANIZATION OF PERSON SIGNING Head of patent department

ADDRESS OF PERSON SIGNING Hofgartenstr. 8, 80539 München

SIGNATURE Christa Herzog DATE 7.6.2000

09/581103  
527 Rec'd PCT/PTO 08 JUN 2000

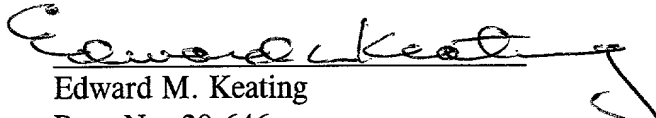
203 Von Bezold  
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Markus Kietzmann and Holger Eickhoff ]

For: Device and Procedure for Image Recording on ]  
Drop-Generating Dispensing Heads ]

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on June 8, 2000.

  
Edward M. Keating  
Reg. No. 20,646

Commissioner of Patents  
and Trademarks  
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Upon the assignment of a serial number and filing date and prior to the examination of this application, please amend it as follows:

In the Specification:

Page 3, line 17, delete "in claims 1, 7, or 9, resp." and insert --herein--.

In the Abstract of the Disclosure:

Last line, delete "(Fig. 1)".

In the Claims:

Cancel claims 1-11 and add the following new claims:

12. An image-recording system for a dispensing head with numerous dispensers, in which a predetermined light path from a lighting device to an image-recording device intersects a drop release area of a drop-releasing dispenser to be detected,

characterized in that a deviating device is provided with which a measuring light segment is formed along a predetermined reference line through said drop release area, and that said lighting and image-recording devices are spaced apart from the said reference line relative to said drop releasing dispenser.

13. The image-recording system according to claim 12, in which said deviating device consists of at least one mirror that is inclined by a first deviating angle relative to said reference line and deflects light from said measuring light segment.

14. The image-recording system according to claim 12, in which said deviating device has two mirrors inclined by a first or second deviating angle relative to said reference line, of which a first mirror deflects light from said lighting device into said measuring light segment, and a second mirror deflects light from said measuring light segment to said image-recording device.

15. The image-recording system according to claim 14, in which said first and second mirrors project into the gaps between said drop-releasing dispenser to be detected and said adjacent dispensers.

16. The image-recording system according to claim 14, in which a third mirror that deflects light from said lighting device to said first mirror is provided, along with a fourth mirror that deflects light from said second mirror to said image-recording device.

17. The image-recording system according to claim 12, in which said lighting device consists of a pulsed light emitted, and said image-recording device has a camera with a lens.

18. A measuring system for recording images of drops on a drop-releasing dispenser to be detected with numerous dispensers of a dispensing head having an image-recording system according to claim 12, in which said lighting and image-recording devices are arranged in a carrier plane over which said dispensing head can traverse, so that the tips of said dispensers move in a reference plane parallel to said carrier plane, wherein said deviating device forms said measuring segment at a perpendicular distance from said carrier plane and directly adjacent to said reference plane.

19. The measuring system according to claim 18, in which the length of said measuring light segment is essentially identical to the distance (d) of adjacent dispensers of said dispensing head.

20. A procedure for recording images of drops on a drop-releasing dispenser of a dispensing head using an image-recording system according to claim 12, in which said

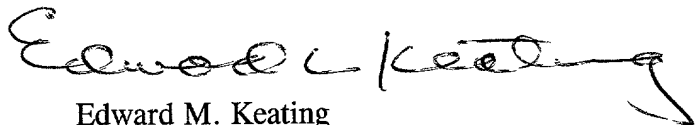
dispensing head is positioned relative to said image-recording system in such a way that said dispenser projects into said measuring light segment.

21. The procedure according to claim 20, in which images are recorded by detecting a sequence of drops with varying delay times between a trigger signal of said dispenser and a trigger signal of said lighting device operated as a stroboscope.

22. The procedure according to claim 20, in which image recording is preceded by a reference image recording with a drop-free measuring segment, and differential images are generated from said recorded drop images and the reference images for image processing.

23. The procedure according to claim 21, in which said image recording is preceded by a reference image recording with a drop-free measuring segment, and differential images are generated from said recorded drop images and the reference images for image processing.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Edward M. Keating". The signature is fluid and cursive, with a long horizontal stroke at the end.

Edward M. Keating  
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Device and Procedure for Image Recording on Drop-Generating  
Dispensing Heads

The invention relates to a device and a procedure for recording drop or particle images on a dispenser head, in particular for stroboscopic image recording of microdrops during formation on a dispenser tip or after release from the latter.

A dispensing head consists of numerous electrically actuatable dispensers (e.g., electrically actuatable micropipettes), which are each set up to release a microdrop in response to an electric trigger signal. To this end, each dispenser has a trigger device that generates a pressure pulse whose parameters depend on the duration and amplitude of the trigger signal.

One important application for dispensing heads lies in the area of biotechnology, genetic engineering or chemical technology, where the goal is to initiate a combined reaction between the smallest quantities of working substances in the form of microdrops on substrates. To ensure that the reaction proceeds efficiently, it is necessary that the microdrops (volumes in the sub-microliter range) be positioned precisely on the reaction substrate with a reproducible drop size and speed. Therefore, there is interest in systems for analyzing and evaluating the drop separation from the dispenser, the direction of drop movement, the drop size and, if necessary, the drop number.



The principle of such a generally known system is shown in Fig. 4 (prior art). An image-recording device 1 consists of a stroboscope lamp 2 and a camera 4. The camera 4 is equipped with a lens (normally a microscope lens) focused on a drop release area located in front of the micropipette tip 5. Extending from the stroboscope lamp 2 to the camera 4 is a light path that crosses the drop release area, so that the camera 4 can record a drop T during separation or in flight. Such an image-recording device is generally provided as a fixed laboratory system to which the dispensing head is moved in such a way that the micropipette tip projects into the light path. The actual expansions of the camera 4 and stroboscope lamp 2 are shown by example with dashed lines. To precisely observe the drops, it is necessary that drop formation take place under constant lighting and image-recording conditions. However, when using multi-channel dispensing heads with numerous planar dispensers, this results in the following problem.

If the dispensers of a multi-channel dispensing head are distributed over a surface whose characteristic expansion is greater than the focal depth of the lens system in the camera 4, an obstruction arises between the dispensing head and the camera setup when positioning a dispenser to be observed in the focal point of the lens, extending into the traveling path of the dispenser (see arrow). The same applies with respect to lighting, since the distance from the stroboscope lamp to the drop must remain as constant as possible. Since the focal depth of the lens system normally ranges from 10 mm to 30 mm, this problem is already encountered at low dispenser numbers on a dispensing head given a dispenser distance of 9 mm, for example. The conventional system fails completely in the case of

dispenser heads wherein dispensers are arranged in matrixes of 4 \* 4 or 8 \* 12 dispenser rows.

WO 97/44134 discloses devices and a procedure for monitoring the microdrop release from pulsed microdrop firing devices. The microdrop release is controlled using a piezoelectric converter. The drop release from microdispensers is also described in the publication by A.V. Lemmo et al. in "Anal. Chem.", Ed. 69, 1997, pp. 543 forward.

The object of the invention is to indicate an improved device for recording drop images, which makes it possible to record an image on multi-channel dispenser heads under conditions that remain constant for all dispensers. The object of the invention is also to indicate a procedure for using such an image-recording device.

This object is solved by devices and a procedure described in claims 1, 7 or 9, resp. Advantageous embodiments of the invention are described in the subclaims.

The invention provides a new image-recording arrangement in which a deviating device modifies the light path from a lighting device to an image-recording device that passes through a drop release area of a drop-releasing dispenser to be observed. The deviating device is provided to guide the light path from the lighting device to the image-recording device over a measuring light segment that is located at a sufficient perpendicular distance from the lighting and image-recording devices, and in which each dispenser of a dispensing head can be freely positioned.

The deviating device consists of at least two reflector elements (mirrors) that fix the measuring light segment. The measuring light segment runs perpendicular to the longitudinal expansion of the dispenser to be measured, and passes by the tip of the respective dispenser, so that a drop can be optically detected immediately after released from the dispenser. Therefore, the reflector elements are designed in such a way that they partially project into the distance between adjacent dispensers of a dispensing head. The reflector elements are arranged in such a way that the light path from the lighting device to the image-recording device runs over the measuring light segment in one plane. The reflector elements form a distance in which the dispenser to be measured can traverse, wherein the drop is released along a straight path running parallel to the measuring light plane.

In a preferred configuration, the lighting and image-recording devices are arranged in a reference plane (e.g., laboratory table plane or the like), which has a perpendicular distance from a reference line formed by the measuring light segment with respect to the longitudinal expansion of the dispensers or drop releasing device. The lighting and image-recording devices include all optical components that provide the measuring light in an area lying under the surface fixed by the dispensers of the dispensing head during image recording in the measuring position.

The subject of the invention is also a procedure for analyzing drop parameters, in which a dispensing head is positioned over an image-recording system with lighting and image recording devices and a deviating device in such a

way that a dispenser to be observed projects into a measuring light segment formed by the deviating device at a distance from the lighting and image-recording devices.

The advantage to the invention is that an image can be recorded for drop analyses on dispenser heads of any size for all dispensers under constant optical conditions. The deviating device of the image-recording system according to the invention makes it possible to freely position the dispensing head relative to the image recording system. The image recording system has a simple structure, and permits a simple correction of any arising image distortions after image recording using an image processor.

Additional details and advantages of the invention will be described below making reference to the attached drawings, which show:

- Fig. 1      a first embodiment of an image-recording system according to the invention,
- Fig. 2      a second embodiment of an image-recording system according to the invention,
- Fig. 3      a third embodiment of an image-recording system according to the invention, and
- Fig. 4      a conventional image-recording system (prior art).

In the following, the invention will be described making reference to a dispenser row, but can also be advantageously used in the same way during the drop

analysis of individual dispensers or planar dispenser groups arranged in matrixes. The invention is not limited to the described stroboscope technique, but can rather be realized with any other image-recording technique that responds quickly enough.

In Fig. 1, an image-recording system 10 encompasses a lighting device 20, a deviating device 30 and an image-recording device 40. The expansion of individual components (e.g., see Fig. 3) is not separately indicated for reasons of clarity. The lighting device 20 contains a stroboscope lamp, e.g., formed by a pulsed, light-emitting diode (LED). The LED is preferably operated at an overvoltage exceeding the normal operating voltage to achieve as high a luminance as possible during pulse operation. The lighting device can also consist of another stroboscope lamp, e.g., in the form of a suitably expanded and pulsed laser. The image-recording device 40 preferably consists of a CCD camera with a microscope lens having a focal depth ranging from 10 mm to 30 mm. However, other detector systems with any cameras (even one-dimensional in the form of a CCD line, if necessary) and normal or macro lenses are possible, whose structure is adapted to the parameter of the drop to be detected.

A lighting light path 21 leads from the lighting device 20 to the deviating device 30, which fixes a measuring light segment 33 that is adjoined by the image-recording light path 41 to the image-recording device 40. The measuring light segment 33 leads through the drop release area through which passes a drop T released from the dispenser 52 to be observed. The measuring light segment 33 leading through the drop release area extends along a reference

line lying in a plane directly adjacent to the surface fixed by the dispenser tips of the dispensing head. While retaining a predetermined lighting distance from the lighting device 20 to the drop T or a predetermined focal distance from the drop T to the image-recording device 40, the deviating device 30 formed by the flat mirrors 31, 32 now makes it possible to position the lighting and image-recording devices at a sufficient distance from the plane in which the reference line lies, or to position them with a sufficient perpendicular distance from the reference line, so that the lighting and image-recording devices do not impede movement of the dispensing head parallel to the mentioned plane.

The mirrors 31, 32 are inclined relative to the measuring light segment 33 by predetermined deviating angles (e.g.,  $45^\circ$ ), and the middles of the mirrors are spaced apart by a distance corresponding to distance d of the dispensers 51, 52, 53, ... of the dispensing head 50. The edges of mirrors 31, 32 to be pointed toward one another are spaced apart, so that a dispenser to be observed can project between the mirrors 31, 32. As a result, the mirrors of the deviating arrangement 30 limit the drop release area of the dispenser. The drops are released in the plane fixed by light paths 21, 33, 41.

In the alternative configuration shown in Fig. 2, the deviating device 30 comprises a mirror 32 inclined relative to the measuring light segment 33, and a mirror 31 sitting perpendicular on the latter. In this case, the lighting light path 21 is identical to the image-recording light path 41. The lighting and image-recording devices 20, 40 are provided with an inclined beam splitter (not shown). As

in the embodiment shown in Fig. 1, the lighting and image-recording devices 20, 40 are spaced apart from the reference plane in which the measuring light segment 33 runs.

In the system according to Fig. 2, the deviating mirror 31 situated parallel on the measuring light segment 33 can be omitted. In this case, the shadow of the backlit drop is not recorded as in Fig. 1, but rather the frontlit image of the drop. In another modification, it is also possible to separate the lighting light path 21 from the image recording light path 41, and allocate the lighting device 20 to a suitable position at a distance from the dispensing head 50. In this case, the deviating device 30 only consist of a flat mirror 32, since the drop recorded with front lighting itself acts as a reflector. Correspondingly, the measuring light segment 33 extends from the drop T to the deviating mirror 32.

Fig. 3 shows another configuration of the invention. The lighting and image-recording devices 20, 40 interact with the deviating mirrors 22, 42. The deviating device 30 otherwise corresponds to the structure according to Fig. 1. The structure according to Fig. 3 is advantageously compatible with conventional image-recording systems (see Fig. 4). The lighting and image-recording devices 20, 40 are arranged on a shared, flat carrier (e.g., laboratory table). The straight light path between both devices is interrupted by the mirror combination 31, 32, 22, 42. Partial light paths are formed, which in particular incorporate the measuring light segment 33 at a distance from the carrier plane. The traveling plane of the dispenser is spaced far enough away from the physical

expansions of the lighting and image-recording devices marked with dashed lines.

To analyze the drop, a dispensing head is positioned in such a way relative to the image-recording system that the measuring light segment passes through the drop release area of a relevant dispenser. When using micropipettes for the above applications, the drop release area can exhibit a characteristic size of roughly 5 mm under the dispensing tip. The length of the measuring segment then measures roughly 10 mm. The diameters of the drops to be detected measure roughly 10  $\mu\text{m}$  to 100  $\mu\text{m}$ . A reference image is first recorded with the dispenser at the measuring position. While recording the reference image, stroboscope flashes of the drop-free light path are taken. For example 10 stroboscope flashes (length roughly 3  $\mu\text{s}$ ) are recorded and stored in an image processing system (not shown). The drop image is then recorded, a process which involves recording images of all phases of drop formation, release and movement for a complete drop analysis. To this end, the dispenser releases a sequence of drops, wherein a delay time between the respective trigger signal of the electrically actuated dispenser and a trigger signal of the stroboscope lighting device is variably set for each drop. Depending on the parameters of the release signal, the delay time can measure up to 500  $\mu\text{s}$ . The sequence of drop images with varying delay times corresponding to the different phases of drop formation is stored and subjected to digitization and image processing that essentially involves working out the difference using the reference images. This compensates for any noise introduced through the mirrors of the deviating device, and any luminescence profile present at the LED of the lighting device. It is



possible to record a group of drop images (e.g., 10) under constant recording conditions (in particular a constant delay time) for each drop formation phase, and accumulate the individual images to improve image quality. The operating frequency of the image-recording device (e.g., image readout frequency to a CCD camera) is then preferably adjusted to the drop frequency in such a way that the drop frequency corresponds to an integer multiple of the operating frequency (e.g.,  $f_{\text{drop}} = 100 \text{ Hz}$ ,  $f_{\text{camera}} = 50 \text{ Hz}$ ).

This is followed by an analysis of the corrected drop images with respect to the drop size (drop volume, working substance amount) and movement properties of the drop. The movement properties include the direction of drop movement and drop speed. If the direction of drop movement does not coincide with the dispenser alignment (e.g., vertical alignment perpendicular to measuring light segment), the dispenser is corrected, or the dispenser tip where solid particles of a working substance might have been deposited is cleaned. The speed is measured by evaluating two drop images of released drops with varying delay times. The drop speed is calculated from the difference in delay times and the corresponding position change. Additional results of the image analysis include the detection of satellite drops or omitted drops, if the dispenser becomes clogged or the release pressure in the dispenser is too low. In addition, it is possible, and in certain applications necessary, to optimize the amplitude and duration of the trigger signal of the dispenser to desired parameters or for quality control by observing the drop properties.

After the parameters of a dispenser have been analyzed, all dispensers of a dispensing head are sequentially moved to

the measuring light segment. The mentioned measuring process is then executed for each of the dispensers.

The positioning of the dispensing head preferably leaves the length of the lighting light path and image recording light path unchanged, so that the drop-generating processes on each of the dispensers can be recorded under identical optical conditions and with a high accuracy and reproducibility.

CLAIMS

(as originally filed and published)

1. An image-recording system (10) for a dispensing head (50) with numerous dispensers (51, 52, 53, ...), in which a predetermined light path from a lighting device (20) to an image-recording device (40) intersects a drop release area of a drop-releasing dispenser (52) to be detected, characterized by the fact that a deviating device (30) is provided with which a measuring light segment (33) is formed along a predetermined reference line through the drop release area, and that the lighting and image-recording devices (20, 40) are spaced apart from the reference line relative to the drop releasing device.
2. The image-recording system according to claim 1, in which the deviating device (30) consists of at least one mirror that is inclined by a first deviating angle relative to the reference line and deflects light from the measuring light segment (33).
3. The image-recording system according to claim 1, in which the deviating device (30) has two mirrors inclined by a first or second deviating angle relative to the reference line, of which a first mirror (31) deflects light from the lighting device (20) into the measuring light segment (33), and a second mirror (32) deflects light from the measuring light segment to the image-recording device (40).

4. The image-recording system according to claim 3, in which the first and second mirrors (31, 32) project into the gaps between the drop-releasing dispenser (52) to be detected and the adjacent dispensers.

5. The image-recording system according to claim 3, in which a third mirror (22) that deflects light from the lighting device (20) to the first mirror (31) is provided, along with a fourth mirror that deflects light from the second mirror (32) to the image-recording device (40).

6. The image-recording system according to one of the preceding claims, in which the lighting device (20) consists of a pulsed light emitted, and the image-recording device (40) has a camera with a lens.

7. A measuring system for recording images of drops on a drop-releasing dispenser (52) to be detected with numerous dispensers of a dispensing head (50) having an image-recording system according to one of claims 1 to 6, in which the lighting and image-recording devices (20, 40) are arranged in a carrier plane over which the dispensing head can traverse, so that the tips of the dispensers move in a reference plane parallel to the carrier plane, wherein the deviating device (30) forms the measuring segment (33) at a perpendicular distance from the carrier plane and directly adjacent to the reference plane.

8. The measuring system according to claim 7, in which the length of the measuring light segment (33) is essentially identical to the distance (d) of adjacent dispensers of the dispensing head.

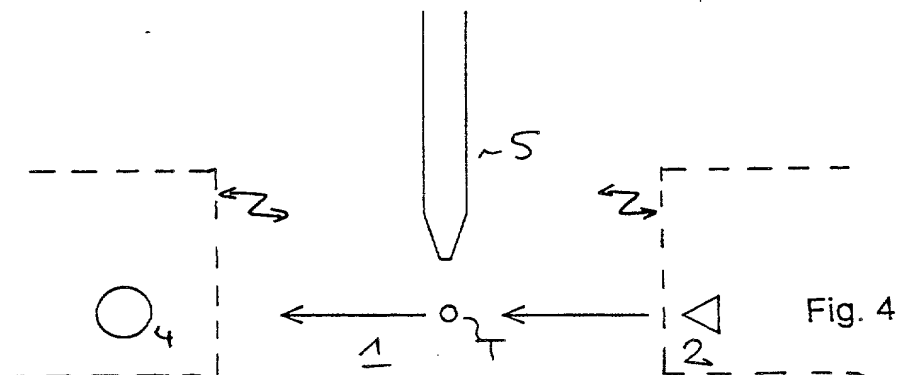
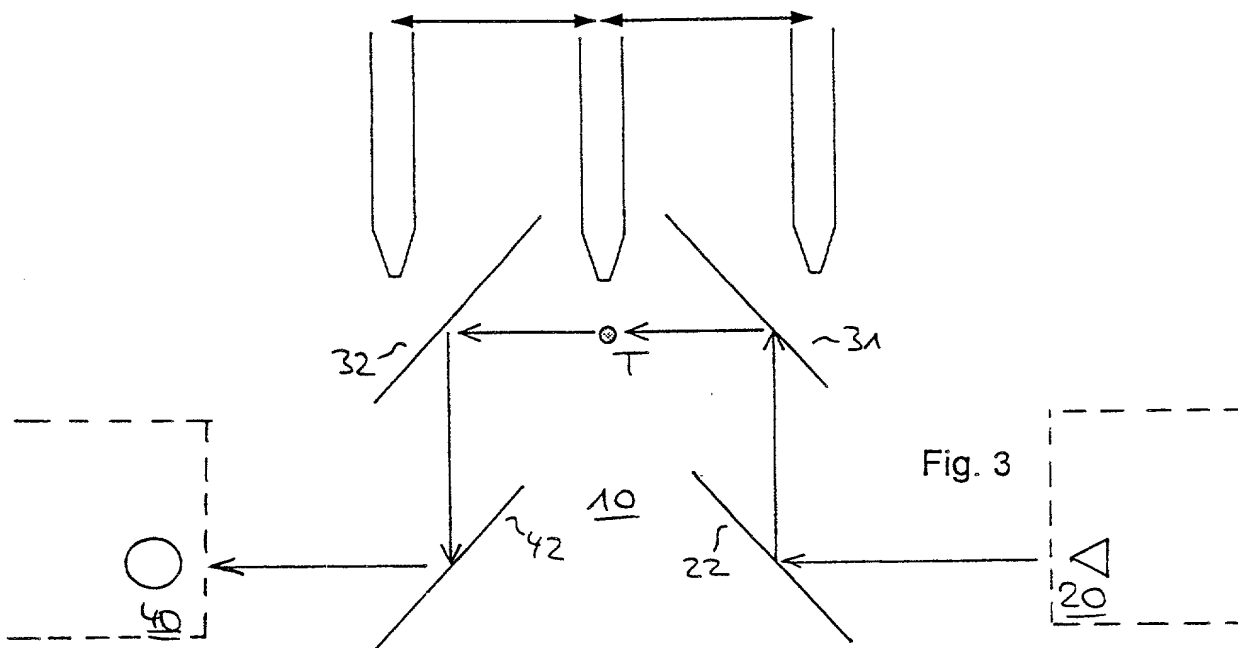
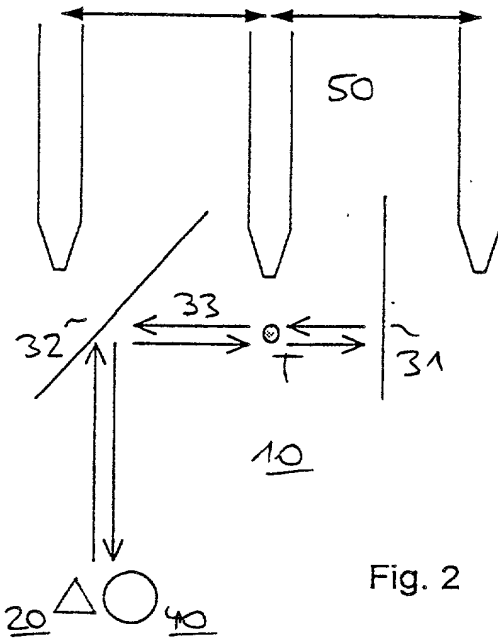
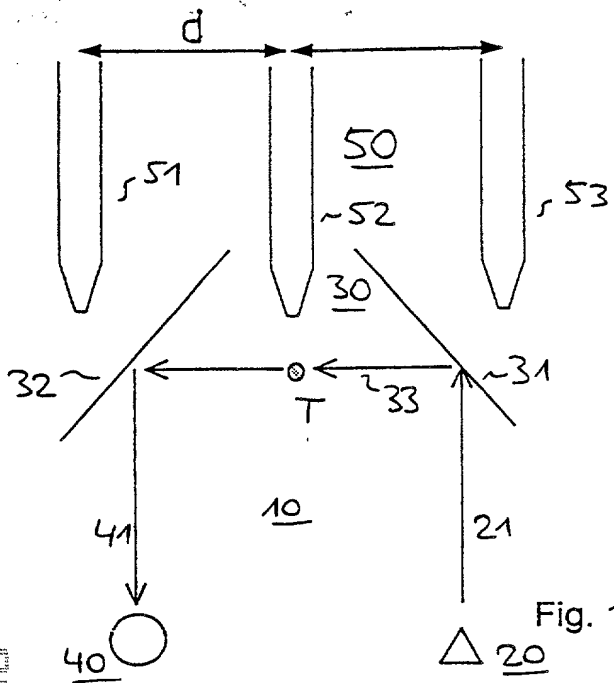
9. A procedure for recording images of drops on a drop-releasing dispenser (52) of a dispensing head (50) using an image-recording system according to one of claims 1 to 6, in which the dispensing head is positioned relative to the image-recording system in such a way that the dispenser projects into the measuring light segment (33).

10. The procedure according to claim 9, in which images are recorded by detecting a sequence of drops with varying delay times between a trigger signal of the dispenser and a trigger signal of the lighting device (20) operated as a stroboscope.

11. The procedure according to claim 9 or 10, in which image recording is preceded by a reference image recording with a drop-free measuring segment, and differential images are generated from the recorded drop images and the reference images for image processing.

## ABSTRACT

(Fig. 1)



- ☐ Original Application
- ☒ PCT National Application  
U.S. Designated Office
- ☐ Continuation or Divisional Application
- ☐ Continuation-in-Part Application

**COMBINED DECLARATION,  
POWER OF ATTORNEY AND PETITION**

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled Device and Procedure for Image Recording on  
Drop-Generating Dispensing Heads

☐ which is described in the specification and claims

☐ attached hereto.

☒ filed on June 8, 2000

Application Serial No. 09/581,103

and was amended on \_\_\_\_\_

*(if applicable)*

☒ which is described in International Application No. PCT/EP98/07952

filed \_\_\_\_\_ and as amended on \_\_\_\_\_


*(if any),*

which I have reviewed and for which I solicit a United States patent.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56.

I do not know and do not believe that this invention was ever known or used in the United States before my or our invention thereof or patented or described in any printed publication in any country before my or our invention thereof or more than one year prior to this application or said international application, or in public use or on sale in the United States of America more than one year prior to this application or said international application, or that the invention has been patented or made the subject of an inventor's certificate issued before the date of this application or said international application in any country foreign to the United States of America on an application filed by me or my legal representatives or assigns more than twelve months prior to this application or said international application, or that any application for patent or inventor's certificate on this invention has been filed in any country foreign to the United States of America prior to this application or said international application by me or my legal representatives or assigns except as identified below.





COMBINED DECLARATION, POWER OF ATTORNEY AND PETITION  
(Page 2)

Attorney Docket No. von Bezold 203

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International Application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application(s) for patent or inventor's certificate or of any PCT International Application having a filing date before that of the application on which priority is claimed:

Number	Country	Date of Filing (day, month, year)	Priority Claimed
Germany		08/12/1997	<input checked="" type="checkbox"/> yes <input type="checkbox"/> no
	PCT/EP98/07952	08/12/1998	<input checked="" type="checkbox"/> yes <input type="checkbox"/> no
			<input type="checkbox"/> yes <input type="checkbox"/> no
			<input type="checkbox"/> yes <input type="checkbox"/> no
			<input type="checkbox"/> yes <input type="checkbox"/> no

I hereby claim the benefit under Title 35, United States Code, §119(e) or §120 (as applicable) of any United States application(s) or §365(c) of any PCT International Application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International Application(s) in the manner provided by the first paragraph of Title 35, United States Code, §112:

<u>(Application Serial No.)</u>	<u>(Filing Date)</u>	<u>(Status) (patented, pending, abandoned)</u>
<u>(Application Serial No.)</u>	<u>(Filing Date)</u>	<u>(Status) (patented, pending, abandoned)</u>

POWER OF ATTORNEY: As a named inventor, I hereby appoint the registered attorneys listed under Customer No. 001517 and the following registered attorneys to prosecute this application and transact all business in the United States Patent and Trademark Office connected therewith:

Daniel C. McEachran, Registration No. 19804; Robert V. Jambor, Registration No. 23080; Edward M. Keating, Registration No. 20646; Joel H. Bock, Registration No. 29045; Vangelis Economou, Registration No. 32341 and Li-Chung Daniel Ho, Registration No. P-41,837, whose address is McEachran, Jambor, Keating, Bock & Kurtz, 55 East Monroe Street, Chicago, Illinois 60603, telephone nos. (312) 726-4421 and 236-1112, as its attorneys, with full power of substitution and revocation.

Edward M. Keating McEachran, Jambor, Keating, Bock & Kurtz 55 E. Monroe Street - Suite 2940 Chicago, IL 60603	DIRECT TELEPHONE CALLS TO ATTORNEY OF RECORD AT: Edward M. Keating 312/726-4421
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COMBINED DECLARATION, POWER OF ATTORNEY AND PETITION  
(Page 3)

Attorney Docket No. von Bezold 203

I hereby petition for grant of a United States Letters Patent on this invention.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

1. FULL NAME OF SOLE OR FIRST INVENTOR <b>KIETZMANN, Markus</b>		INVENTOR'S SIGNATURE <i>Markus Kietzmann</i>	DATE 07.06.00
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RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
5. FULL NAME OF ADDITIONAL JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
6. FULL NAME OF ADDITIONAL JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
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RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			

COMBINED DECLARATION, POWER OF ATTORNEY AND PETITION  
(Page 3)

Attorney Docket No. von Bezold 20

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
5. FULL NAME OF ADDITIONAL JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
6. FULL NAME OF ADDITIONAL JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			
7. FULL NAME OF ADDITIONAL JOINT INVENTOR, IF ANY		INVENTOR'S SIGNATURE	DATE
RESIDENCE		CITIZENSHIP	
POST OFFICE ADDRESS			